From the Society for Vascular Surgery

Characterization of retrograde collateral (type II) endoleak using a new canine model

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Objective: **The clinical significance of retrograde collateral arterial perfusion of abdominal aortic aneurysms after endovascular repair (type II endoleak) has not been completely characterized. In this study a canine model was used to analyze intra-aneurysmal pressure, thrombus histologic characteristics, endoleak patency, and radiographic appearance of type II endoleaks originating from single and multiple aneurysm side branches.**

Methods: **Prosthetic aneurysms with an intraluminal solid-state strain-gauge pressure transducer were created in the infrarenal aorta of 14 mongrel dogs. A single collateral side branch was reimplanted in 4 animals, multiple side branches were reimplanted in 6 animals, and no side branches were reimplanted in 4 control animals. Intra-aneurysmal and systemic pressure was measured for 60 to 90 days after creation of the type II endoleak. Endoleak patency and flow were assessed with duplex ultrasound scanning and cine–magnetic resonance angiography. Histologic analysis of the intra-aneurysmal thrombus was also performed.**

Results: **Stent-graft exclusion reduced intra-aneurysmal pressure significantly in all animals, as compared with systemic pressure ($P < .001$). All intra-aneurysmal pressure values are indexed to the systemic pressure, and are represented as a percentage of the simultaneously obtained systemic pressure, which has a value of 1.0. Type II endoleaks originating from multiple side branches exhibited significantly increased intra-aneurysmal systolic pressure, mean pressure, and pulse pressure, as compared with endoleaks derived from either a single side branch (systolic pressure: multiple, 0.70 ± 0.28 vs single, 0.50 ± 0.19; $P < .001$; mean pressure: multiple, 0.78 ± 0.23 vs single, 0.59 ± 0.22, $P < .001$; pulse pressure: multiple, 0.41 ± 0.25 vs single, 0.17 ± 0.15, $P < .001$) or excluded control aneurysms that had no side branches and no endoleak (systolic pressure, 0.17 ± 0.09; mean pressure, 0.14 ± 0.10; pulse pressure, 0.098 ± 0.08; $P < .001$). Cine–magnetic resonance angiograms and duplex ultrasound scans documented persistent patency of multiple branch endoleaks up to the time of euthanasia. In contrast, single side branch endoleaks thrombosed within 3 days ($P < .001$). Thrombus in the aneurysm sac in close proximity to the endoleak contained intact red blood cells and limited fibrin. Thrombus distant from the endoleak demonstrated extensive fibrin deposition and degraded red blood cells.**

Conclusion: **The canine model may be used to reliably measure intra-aneurysmal pressure in the presence of patent and thrombosed type II endoleaks. In this model 2 or more side branches are necessary to maintain persistent patency of type II endoleaks. These endoleaks are associated with significantly elevated intra-aneurysmal pressure, that is, 70% to 80% of systemic pressure. These results suggest that persistent type II endoleaks have clinical significance. (J Vasc Surg 2004;40:985-94.)**

Clinical Relevance: **Endoleaks originating from retrograde flow in the side branch vessels of the aneurysm generate significant levels of intra-aneurysmal pressure, that is, 70% to 80% of systemic pressure. At least 2 patent side branch vessels appear to be necessary to cause persistent patency of type II endoleak in the canine model. Further studies will be necessary to enable more complete characterization of retrograde endoleaks and to extend these findings to allow clinical application. However, these results suggest that persistently patent type II endoleaks are of clinical significance and may require more intensive follow-up or intervention.**

Endovascular treatment of abdominal aortic aneurysm (AAA) is predicated on exclusion of the aneurysm from the arterial circulation.[1] Exclusion eliminates arterial flow and pressure from the aneurysm sac to prevent continued aneurysm expansion and rupture. Continued arterial perfusion of the aneurysm sac after endovascular treatment may com-

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Supported by National Institutes of Health Grant K08 HL73313-01.
Competition of interest: none.
Presented at the 2004 Lifeline Foundation, Joan L. and Julius Jacobson Research Initiatives in Vascular Surgery Conference, Bethesda, Md, Apr 1-2, 2004.

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0741-5214/$30.00

doi:10.1016/j.jvs.2004.07.049

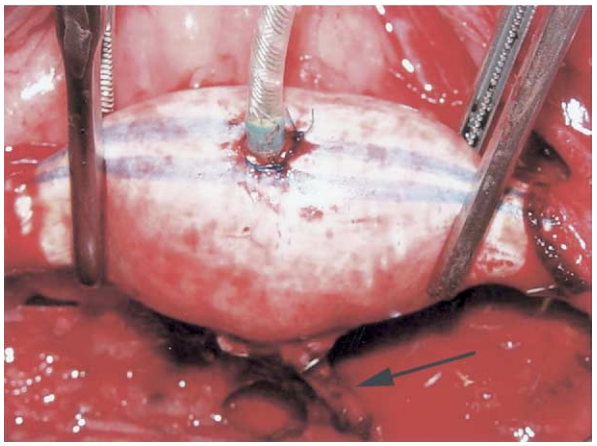

Fig 1. Intraoperative photograph of aneurysm creation. Lumbar arteries *(arrow)* have been anastomosed to the posterior aspect of the prosthetic aneurysm with a Carrel patch. Pressure transducer cable can be seen exiting the anterior aspect of the aneurysm.

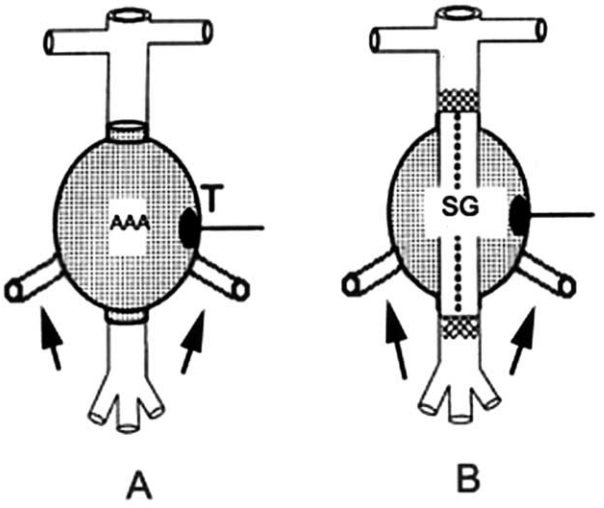

Fig 2. Schematic of retrograde (type II) endoleak creation. **A,** Prosthetic aneurysm *(AAA)* is sewn as an interposition graft in the infrarenal aorta. Paired lumbar arteries *(arrows)* are reimplanted onto the aneurysm as a Carrel patch. Strain-gauge pressure transducer *(T)* enables intra-aneurysmal pressure determination. Pressure transducer is 3 mm in diameter and 1 mm deep. **B,** Retrograde (type II) endoleak is created by deploying a stent graft *(SG)* coaxially through the aneurysm to exclude it from antegrade perfusion.

promise the effectiveness of endovascular aneurysm repair. Continued aneurysm perfusion after endovascular repair has been reported in 14% to 29% of patients in clinical trials.[2-8] This continued arterial perfusion has been termed "endoleak," and may be broadly categorized as originating from either a direct antegrade or retrograde collateral source.[9,10] Antegrade perfusion results in transmission of systemic arterial pressure to the aneurysm sac and continued risk for aneurysm rupture. Antegrade endoleak therefore mandates repair at the time of initial diagnosis.

In contrast, endoleaks that originate from retrograde flow through collateral vessels into aneurysm side branch arteries and the aneurysm sac are of undetermined significance.[11-13] The pressure and force associated with retrograde perfusion of the aneurysm sac has been incompletely characterized. The risk for continued aneurysm expansion and for aneurysm rupture has not been definitively established.[14,15] Attempts to measure intra-aneurysmal pressure resulting from retrograde perfusion of the aneurysm have been hindered by the challenges of accessing an aneurysm that has been excluded from antegrade flow and by limitations of the accuracy of hydrostatic column pressure transducers in measuring pressure through semisolid material such as the thrombus contained within aneurysms.[16] Consequently, definitive conclusions regarding the risks and management of retrograde endoleaks have not been established. In this study a canine model was developed to evaluate continued aneurysm perfusion after endovascular treatment that occurred through retrograde flow in collateral aneurysm side branch vessels, type II endoleaks. Retrograde endoleaks were characterized with regard to the resultant intra-aneurysmal pressure generated, effect of the number of feeding side branch vessels on intra-aneurysmal pressure and endoleak patency, histologic characterization of the intra-aneurysmal thrombus, and radiographic appearance at magnetic resonance imaging (MRI).

MATERIAL AND METHODS

Animals and implantation. Prosthetic aneurysms were created in the infrarenal aorta of 14 mongrel dogs. All animals were treated in accordance with the *Guide for the Care and Use of Laboratory Animals* formulated by the Institute of Laboratory Animal Resources, Commission on Life Sciences.[17] Animals weighed between 25 and 30 kg. After induction of general anesthesia (induction, thiopental 8 mg/kg intravenously; maintenance, isoflourane 2%) transabdominal exposure of the aorta was performed. Systemic anticoagulation (unfractionated sodium heparin, 2000 units intravenously) was maintained throughout the period of arterial clamping. The prosthetic aneurysm containing the intraluminal pressure transducer was implanted as an interposition graft in the infrarenal aorta (Fig 1). Care must be taken to ensure that no damage is done to the adjoining retroperitoneal structures, such as the ureters. Use of male animals is advantageous to avert surgical complexities related to the canine uterus. Collateral side branch vessels were reimplanted onto the aneurysm with a Carrel patch technique (Fig 2). Minimal handling of the lumbar vessels is important, to minimize the risk for vasospasm or intimal injury to the lumbar arteries. In 4 animals a single lumbar artery was reimplanted onto the aneurysm. In 6 animals multiple side branch vessels were reimplanted. Of these 6 animals, 4 animals had reimplantation of 2 paired lumbar arteries, whereas in 2 animals the caudal mesenteric artery was reimplanted in addition to 2 lumbar arteries. No side branch arteries were reimplanted in 4 animals; these

served as control aneurysms with no endoleak. The cable from the pressure transducer was tunneled laterally through the abdominal wall and tracked subcutaneously to exit the skin on the posterior aspect of the neck. Addition of a protective collar aids in enabling the transducer site to heal and to prevent manipulation by the animal. A second implantable pressure transducer was placed in the native aorta proximal to the aneurysm, and tunneled along a parallel course, exiting the skin in the neck adjacent to the first transducer. Measurements from both transducers were obtained simultaneously to enable comparison of intra-aneurysmal pressure and systemic arterial pressure.

Pressure transducer and prosthetic aneurysm creation. An implantable, solid-state, strain-gauge pressure transducer (Konigsberg Instruments) was used for chronic in vivo monitoring of intra-aneurysmal pressure (Fig 3). The transducer is highly accurate in measuring pressure in a wide range of physiologic applications, including intracardiac, intracecal, and intravascular thrombus. The transducer is used in conjunction with data recording software, which is the proprietary property of Data Integrated Scientific Systems. Continuous pressure monitoring and storage were performed with the Data Integrated Scientific Systems software. The accuracy of the transducer has also been confirmed in various media in vitro, including liquid, gelatinous, and solid environments.[18,19] Calibration of the transducer should be preformed before implantation and after explantation. The pressure transducer was approximated to the luminal surface of the prosthetic aneurysm. Prosthetic aneurysms were created by balloon dilation of an 8-mm polytetrafluoroethylene (PTFE) conduit (Impra; Bard Corp). The PTFE material was not altered, and no layers of the graft were removed before dilation with the balloon. The final aneurysm diameter was 30 mm (Fig 4).

Creation of retrograde (type II) endoleak. After implantation of the aneurysm containing the pressure transducer and side branch arteries, intra-aneurysmal pressure determinations were made daily for 2 weeks. Exclusion of the aneurysm sac from antegrade perfusion was then performed. An impermeable endovascular stent graft constructed from PTFE supported throughout its entire length by nitinol stents (Viabahn endoprosthesis, W. L. Gore; 8 mm in diameter × 5 cm long, 2 prostheses per aneurysm exclusion deployed in an overlapping fashion through a 9F sheath) was implanted transarterially via femoral access. Because of the small size of the canine femoral arteries relative to the large introducers necessary for stent-graft deployment, open surgical exposure of the femoral arteries is necessary. Intraoperative angiography was performed through the contralateral femoral artery. Puncture of the femoral arteries should be performed before creation of the arteriotomy to prevent subintimal dissection. Continued patency and retrograde flow in the aneurysm side branch arteries was confirmed on angiograms after stent-graft deployment excluded the aneurysm from antegrade arterial flow. After stent-graft deployment intra-aneurysmal pressure was determined continuously for 4 hours, then daily for 60 to 90 days, until euthanasia of the animal (mean, 71 days after type II endoleak creation). Most animals were euthanized 60 days after type II endoleak creation; however, observations of 2 animals with multiple side branches were continued for 90 days. No alterations in endoleak patency or intra-aneurysmal pressure occurred during the additional 30 days of observation.

Fig 3. Implantable strain gauge pressure transducer. Tip of pressure transducer is attached to the luminal surface of the aneurysm.

Systemic pressure was obtained simultaneously with the second transducer, which was implanted in the native aorta. Intra-aneurysmal pressure was indexed to systemic arterial pressure, and is reported as a percentage of systemic pressure. In addition, systemic pressure measurements were confirmed with a forelimb sphygmomanometer at the same setting. Correlation of the sphygmomanometer with intra-arterial pressure was highly accurate. Clopidogrel (75 mg/d) was administered to all animals after deployment of the endovascular stent graft, to enhance retrograde endoleak patency.

Radiologic imaging. Radiologic evaluation was used to assess patency of the reimplanted aneurysm side branches and endoleak. At endografting, arteriography was performed to demonstrate patency and direction of flow in the aneurysm side branch arteries (lumbar, caudal mesenteric). At euthanasia selective canulation of the side branch arteries was performed and selective arteriography was carried out to evaluate retrograde endoleak patency and to characterize the direction of flow in the side branch vessels and aneurysm sac.

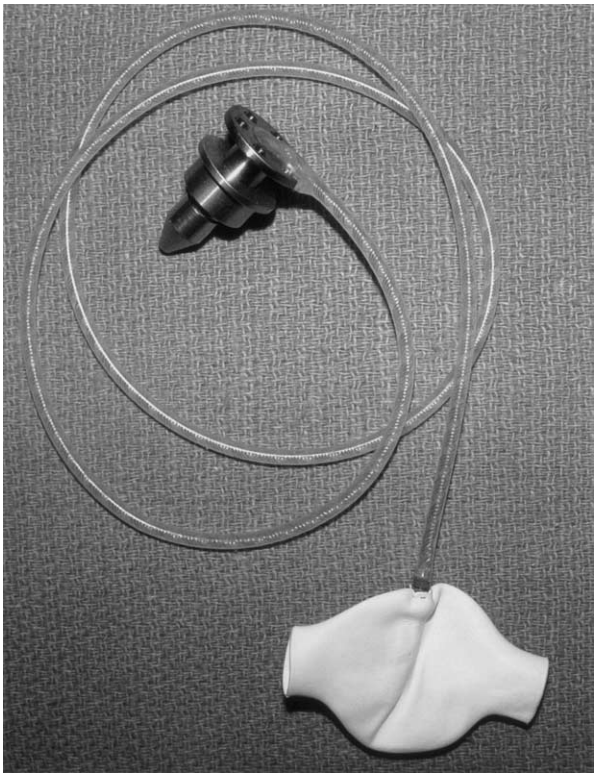

Fig 4. Prosthetic aneurysm with implanted pressure transducer. Transducer cable is tunneled laterally through the abdominal wall and tracked subcutaneously to exit the skin on the posterior aspect of the neck.

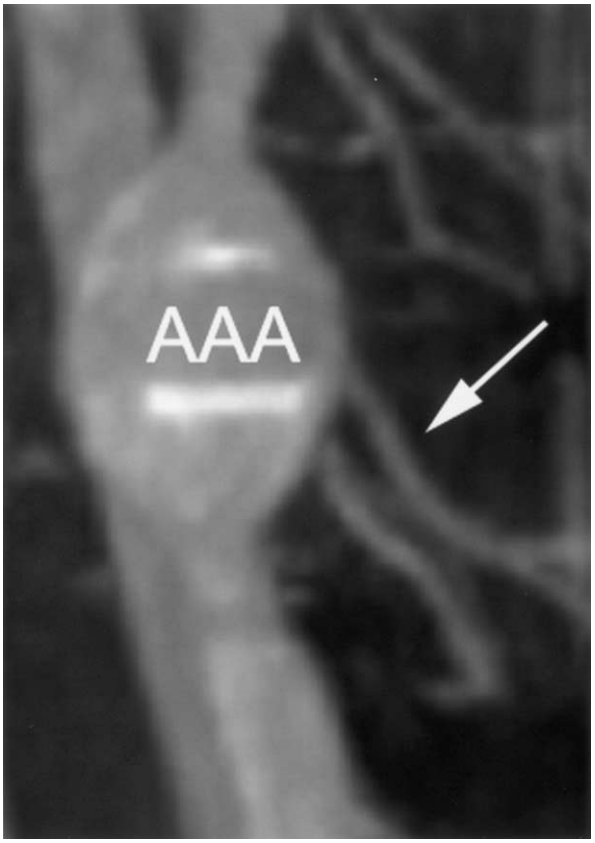

Fig 5. Three-dimensional reconstruction magnetic resonance image with gadolinium enhancement. Paired lumbar arteries *(arrow)* are reimplanted onto the aneurysm sac *(AAA)*. The inferior vena cava is also visualized.

Magnetic resonance angiography (MRA) was performed after initial creation of the aneurysm, using cine sequences (Fig 5). High-field 3-dimensional MRIs and electrocardiogram-gated cine-MRA images were obtained with a 3.0-T system (GE Medical Systems). Images were obtained in the coronal, axial, and sagittal planes, and were used to plan subsequent imaging in the axial plane for cine-gating MRA. Fast cine-echo sequences were used before and after exclusion to study the patency of the lumbar vessels and to characterize the intra-aneurysmal thrombus. Gadodiamide (20 mL; Amersham Health) was injected, followed by 10 mL of normal saline solution flush, with the injection timed to terminate at the beginning of image acquisition. Initial images were obtained with cardiac-gated, gradient-echo acquisition fast-spoiled gradient-recalled acquisition protocol. Induction of general anesthesia is necessary to control the animal's respirations and to prevent movement artifact.

Cine-MRA was performed again at 2, 4, and 6 weeks after aneurysm exclusion with stent-graft deployment, to assess the type II endoleak. Patency of the side branch arteries with persistent retrograde perfusion of the aneurysm sac was again studied. Duplex ultrasound scanning of arterial flow in the aneurysm sac and in the side branch arteries was performed intraoperatively before and after antegrade exclusion. In animals with single side branch endoleaks, duplex scanning was repeated 1, 2, and 3 days after creation of the type II endoleak. Duplex ultrasound scanning was performed at euthanasia to again assess side branch patency and retrograde aneurysm perfusion.

Histologic and pathologic analysis. The AAA, including the side branch arteries and the stent graft, was perfusion-fixed at 100 mm Hg in 3% glutaraldehyde buffered to pH 7.4 with sodium cacodylate. At euthanasia the aorta was clamped proximally and distally to the aneurysm. The aneurysm and side branch vessels were then removed en bloc for gross and microscopic pathologic analysis. The aneurysms were sectioned longitudinally, and the stent graft was removed. After dehydration in increasing concentrations of ethyl alcohol, representative sections were imbedded in paraffin. Longitudinal, transverse, and oblique sectioning was performed, and microscopic analysis was carried out with hematoxylin-eosin stain. The stent graft was removed before sectioning, because the microtome blade could not cut the nitinol wire. Histologic interpretation was conducted independently by a pathologist (R.G.) blinded to the origin of the histologic section.

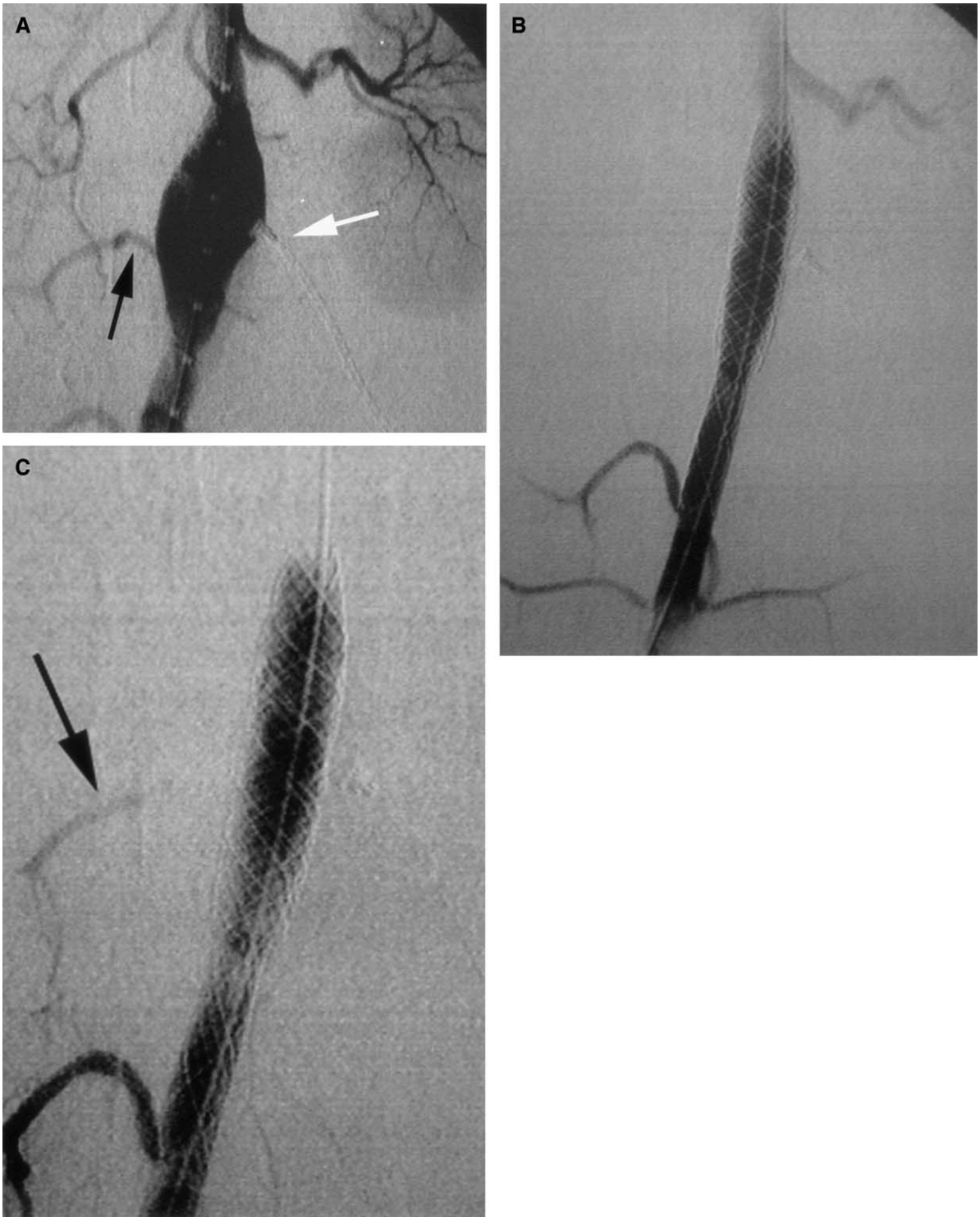

Fig 6. Intraoperative digital subtraction angiogram of stent-graft deployment to create retrograde (type II) endoleak. **A,** Before deployment of the stent graft, arterial flow enters the reimplanted lumbar arteries *(black arrow)* from the aneurysm sac in an antegrade fashion. Strain-gauge pressure transducer *(white arrow)* can be seen exiting the aneurysm laterally. **B,** After stent-graft deployment the aneurysm is excluded from antegrade arterial perfusion. **C,** Angiographic image obtained after 8-second delay demonstrates retrograde opacification of the reimplanted lumbar artery *(arrow)* leading to retrograde aneurysm perfusion (type II endoleak).

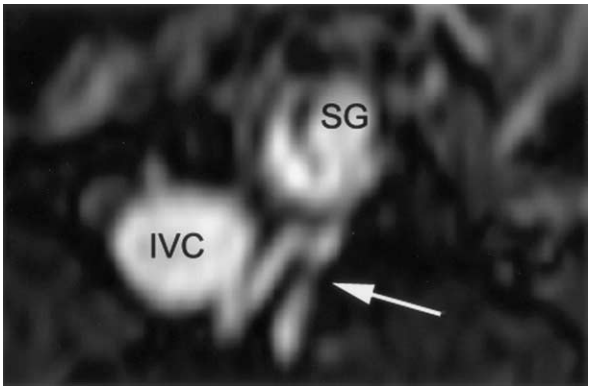

Fig 7. Magnetic resonance image with gadolinium enhancement of retrograde (type II) endoleak. Paired lumbar arteries *(arrow)* are visualized perfusing the aneurysm sac in a retrograde manner. Stent graft *(SG)* is seen within the aneurysm sac. Inferior vena cava *(IVC)* is also visualized.

Statistical analysis. All intra-aneurysmal pressure measurements were indexed to the systemic pressure, which was obtained simultaneously. All pressures are represented as a percentage of the systemic pressure, with the systemic pressure having a value of 1.0. Continuous variables were analyzed with the Student *t* test. Discrete variables were analyzed with χ^2 analysis. Statistical significance was assumed at $P \leq .05$.

RESULTS

Endoleak patency and flow assessment. Aneurysm side branch patency and retrograde endoleak patency were confirmed on intraoperative angiograms in all animals at the time of exclusion of the aneurysm from antegrade flow by stent-graft deployment (Fig 6). In all animals complete exclusion from antegrade perfusion was achieved, and therefore no type I endoleaks were present. Animals with multiple aneurysm side branches (2 lumbar, with or without caudal mesenteric arteries) demonstrated persistent side branch and endoleak patency throughout the study. Retrograde endoleak patency was confirmed with cine-MRA (Fig 7) and duplex ultrasound scanning in animals with aneurysms with multiple side branches. Angiography performed by selective cannulation of the caudal mesenteric artery at euthanasia demonstrated retrograde flow in the caudal mesenteric artery. This arterial flow resulted in retrograde perfusion of the aneurysm sac, with contrast pooling external to the stent graft. Arterial flow exited the aneurysm sac through the paired lumbar arteries. This finding was confirmed at cine-MRA in this animal. Therefore patency was maintained, with flow entering the aneurysm sac through retrograde flow in the caudal mesenteric artery and emptying through to the lumbar artery.

In contrast, animals with aneurysms containing a single side branch demonstrated thrombosis of the endoleak that occurred within 3 days (mean, 2.3 days) of type II endoleak creation. Arterial flow in the side branch and retrograde

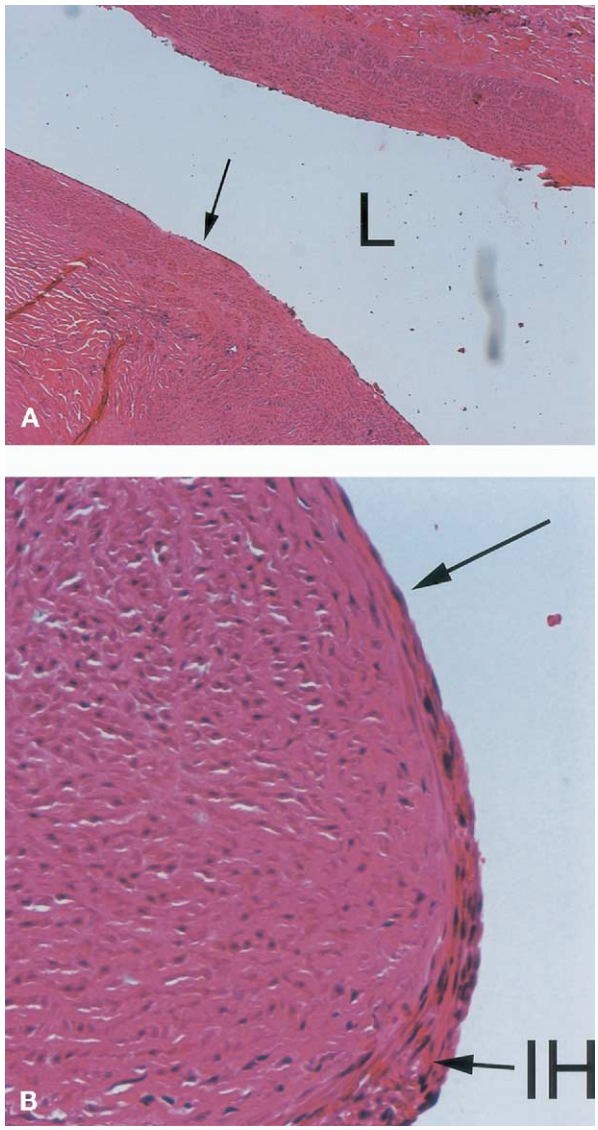

Fig 8. Photomicrograph of lumbar artery and anastomosis to prosthetic aneurysm. **A,** At low-power magnification viable endothelial cells *(arrow)* are lining the lumen *(L)* of the patent lumbar artery (hematoxylin-eosin stain; original magnification ×40). **B,** At higher magnification, anatomy of endothelial cells *(arrow)* is more readily seen. Minimal intimal hyperplasia *(IH)* is present at the anastomosis to the aneurysm.

aneurysm perfusion were confirmed absent at cine-MRA and duplex ultrasound scanning. This difference in side branch and endoleak patency was statistically significant ($P < .001$).

Intra-aneurysmal pressure. After the stent graft was deployed and antegrade perfusion of the aneurysm was eliminated, intra-aneurysmal pressure was significantly reduced within 3 hours in all animals ($P < .001$; Table). After the initial decline in intra-aneurysmal pressure, pressure measurements remained stable throughout the study (60-90 days). All

Table I. Intraaneurysmal pressure analyzed by number of aneurysm side branch arteries contributing to retrograde (type II) endoleak

	*Systolic pressure**	*Mean pressure**	*Pulse pressure**
Multiple branches	0.70 ± 0.28	0.78 ± 0.23	0.41 ± 0.25
Single branch	0.50 ± 0.19	0.59 ± 0.22	0.17 ± 0.15
Control (no branch)	0.17 ± 0.09	0.14 ± 0.10	0.098 ± 0.08
Systemic pressure	1.0	1.0	1.0
P (single vs multiple aneurysm side branches)	<.001	<.001	<.001

*All pressures listed were measured after creation of type II endoleak, and are indexed as a percentage of systemic pressure.

data presented represent the average plus or minus the standard deviation for the entire post-exclusion period. In aneurysms with multiple side branches the systolic pressure within the aneurysm sac after antegrade exclusion was 0.702 ± 0.283, versus 1.0 for systemic pressure ($P < .001$). Similarly, mean intra-aneurymal pressure after antegrade exclusion for multiple side branch aneurysms was reduced to 0.784 ± 0.229, compared with 1.0 for systemic pressure ($P < .001$). Pulse pressure within the multiple side branch aneurysms was most significantly reduced by exclusion from antegrade perfusion (0.406 ± 0.248 vs 1.0; $P < .001$). There was no difference in intra-aneurysmal pressure between endoleaks originating from 2 as compared with 3 side branches (systolic pressure: 2 branches, 0.705 ± 0.285 vs 3 branches, 0.701 ± 0.302, $P =$ NS; mean pressure: 2 branches, 0.804 ± 0.241 vs 3 branches, 0.797 ± 0.223, $P =$ NS).

Aneurysms with type II endoleaks that originated from a single side branch exhibited a greater reduction in intra-aneurysmal pressure. The reduction in intra-aneurysmal pressure began intraoperatively at endovascular stent-graft deployment. Intra-aneurysmal pressure reached stable levels within 3 hours of exclusion from antegrade perfusion. This reduction in intra-aneurysmal pressure was significantly lower than the pressure observed in aneurysms with multiple side branches contributing to retrograde endoleak. The indexed systolic intra-aneurysmal pressure for single side branch endoleaks was 0.502 ± 0.19, versus 0.702 ± 0.283 for multiple side branch endoleaks ($P < .001$). Similarly, the reduction in mean intra-aneurysmal pressure (single, 0.593 ± 0.215 vs multiple, 0.784 ± 0.229; $P < .001$) and intra-aneurysmal pulse pressure (single, 0.168 ± 0.154 vs multiple, 0.406 ± 0.248; $P < .001$) was significantly greater for aneurysms with a single side branch as compared to those with multiple side branches contributing to retrograde endoleak. Intra-aneurysmal pressure declined again after endoleak thrombosis, which occurred at a mean of 2.3 days after endoleak creation. After thrombosis intra-aneurysmal pressure was indistinguishable from that observed in control aneurysms. Control animals with aneurysms that had no side branches or endoleaks exhibited the lowest intra-aneurysmal pressure after exclusion from antegrade perfusion (systolic pressure, 0.172 ± 0.091; mean pressure, 0.137 ± 0.102; pulse pressure, 0.098 ± 0.077).

Pathologic and qualitative histologic analysis. Gross pathologic analysis confirmed patency of the side branch vessels and the endoleak channel in aneurysms with retrograde endoleaks originating from multiple side branches. Occlusion of the side branch vessel in aneurysms with a single side branch was also confirmed at gross pathologic analysis. Microscopic analysis of the lumbar arteries causing multiple side branch type II endoleaks demonstrated a widely patent lumen lined by viable endothelial cells (Fig 8). Minimal intimal hyperplasia was present at the site of anastomosis to the aneurysm.

Significant variation in thrombus consistency was observed within the aneurysm sac in animals with multiple side branch retrograde endoleaks. In regions of the aneurysm sac distant from the retrograde endoleak and patent lumbar and caudal mesenteric arteries, greater thrombus density with extensive fibrin deposition and degraded red blood cells was observed (Fig 9). These findings were suggestive of stable thrombus, with deposition occurring significantly earlier. In contrast, regions of the aneurysm sac in close proximity to the patent side branch arteries had thrombus that contained intact red blood cells and limited fibrin. Active remodeling with recent thrombus deposition in close proximity to the patent side branches was suggested by these findings.

DISCUSSION

Use of animal models to study endovascular treatment of AAA preceded the initial reports of successful clinical use.[1] Initial animal studies evaluated the feasibility of stent-graft implantation and endovascular aneurysm repair.[20-22] Subsequently animal models have been used in a range of experiments designed to provide further objective scientific assessment of endovascular treatment of AAA.[23-32] The results of these laboratory studies influenced the clinical management of patients with AAA with stent grafts. However, these studies have been limited in evaluating the effects of retrograde collateral perfusion of the aneurysm sac after treatment with a stent graft.[1] The current model allows for creation of a retrograde (type II) endoleak in a model with continuous intra-aneurysmal and systemic pressure measurement. In addition, the effects of retrograde flow on intra-aneurysmal pressure, as well as the radiographic appearance and histologic characterization of the intra-aneurysmal thrombus is characterized. This combination of analyses makes the current model unique among animal models. Animal experiments have provided evidence indicating that continued aneurysm perfusion that

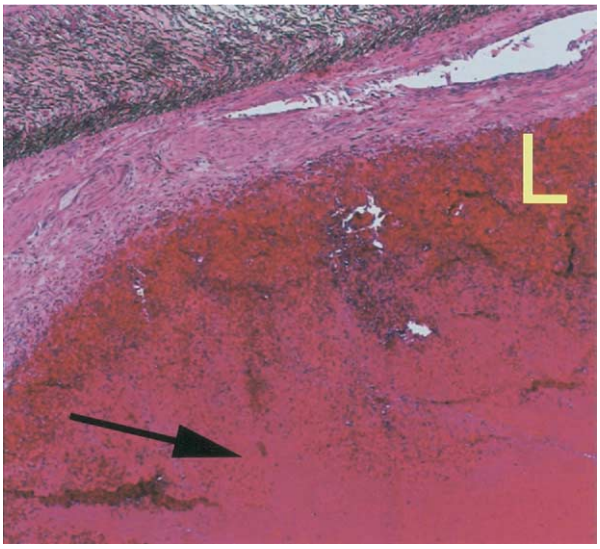

Fig 9. Photomicrograph of aneurysm content. In close proximity to retrograde endoleak and patent side branch arteries the intra-aneurysmal thrombus is comprised predominately of intact red blood cells with limited fibrin deposition *(L)*. In regions of the aneurysm distant from the endoleak *(arrow)* greater thrombus density, with extensive fibrin deposition and degraded red blood cell fragments, is present.

originates from an antegrade source, such as an attachment site (type I) or a graft junction site (type III), are associated with systemic pressurization of the aneurysm sac and high risk for aneurysm rupture.[33] Ex vivo analyses of endoleaks and aneurysm perfusion have also contributed significantly to the understanding of the effect of endovascular repair of AAA.[34-36]

Significant elements of endovascular repair of AAA remain incompletely characterized in previous ex vivo and animal model analyses, however. The effect of retrograde perfusion of the aneurysm sac that occurs through collateral aneurysm side branches such as the lumbar and inferior mesenteric arteries after antegrade aneurysm exclusion is principal among these. Studies of clinical assessment of intrasac pressure have reported varied results. Direct catheter access of the aneurysm sac has indicated that significantly elevated pressures may result from continued retrograde perfusion after endovascular repair.[12] Instances of continued aneurysm expansion and even aneurysm rupture resulting from retrograde endoleaks have also been reported.[14,15] However, in most cases reported, stabilization of aneurysm size has been noted.[37,38] In addition, the success of treatments designed to thrombose type II endoleaks has been variable.[39] The potential for intermittent patency or visualization of type II endoleaks has also been reported.[40] The current study used a canine AAA model with a pressure transducer implanted over a prolonged period to evaluate the pressure generated within the aneurysm sac by type II endoleaks. The transducer is constructed from solid-state components, and uses a strain-gauge to monitor intra-aneurysmal pressure. The transducer has been evaluated in a range of ex vivo and in vivo settings.[18,19,29] It has demonstrated a high degree of accuracy in liquid, semisolid, and solid media, including flowing blood, thrombus, gelatin, intramural cardiac tissue, and cecal contents. These features contributed significantly to the ability to accurately assess the intra-aneurysmal pressure in the presence of thrombus in this study.

The effect of the number of aneurysm side branches on endoleak patency was significant in the current study. Animals that had multiple side branch arteries demonstrated continued patency of the type II endoleak throughout follow-up, which ranged from 60 to 90 days. In contrast, animals with a single arterial vessel supplying the retrograde endoleak experienced rapid thrombosis of the endoleak, within 3 days after endoleak creation. For endoleaks originating from multiple side branches, arterial flow was documented to enter the aneurysm sac through one vessel and to exit the aneurysm sac through a second, distinct vessel. On the basis of these findings, it appears that at least 2 side branches are necessary to enable flow through the aneurysm sac and to prevent thrombosis of the endoleak. These findings may have implications for clinical management of persistent type II endoleaks. If 2 or potentially more patent side branches are necessary to enable flow through the aneurysm sac, treatment success may be increased by identification of the inflow and outflow vessels. Cine-MRA was valuable in confirming type II endoleak patency or thrombosis in the study animals. These findings may also provide a rationale for inducing thrombosis within the aneurysm sac in addition to the side branch vessels.

The pressure generated by retrograde aneurysm perfusion varied according to the number of vessels contributing to the endoleak. In aneurysms with 2 or 3 side branches contributing to retrograde perfusion, intra-aneurysmal pressure was maintained at greater than 70% of systemic pressure. Of note, there was no difference in the intra-aneurysmal pressure generated by retrograde perfusion originating from 2, as compared with 3, side branch vessels. This level of intra-aneurysmal pressure appears to be significant, although further studies will be necessary to adequately characterize the clinical effects and implications. In contrast to aneurysms with multiple side branches, aneurysms with retrograde endoleaks that originated from a single side branch artery had significantly lower intra-aneurysmal pressures, less than 60% of systemic pressure. In addition, once thrombosis of the single side branch endoleak occurred, intra-aneurysmal pressure dropped to less than 15% of systemic pressure. That pressure was equal to the intra-aneurysmal pressure observed in the control animals, with aneurysms with no side branches and no endoleaks. This finding may suggest that the detection of persistent pressurization of the aneurysm sac in patients without an obvious endoleak may indicate an occult source of arterial perfusion and that more aggressive attempts at localization could be considered. Other sources of endotension, including hygroma and sac infection, should also be evaluated.

Characterization of the intra-aneurysmal thrombus in animals with multiple arterial side branches and persistently

patent type II endoleaks demonstrated significant variation that correlated with the location in the aneurysm sac. In regions distant from the patent side branches and endoleak the thrombus had greater density, with extensive fibrin deposition. There were few intact red blood cells and predominately red blood cell fragments. In contrast, thrombus in close proximity to the endoleak and retrograde flow from the side branch arteries exhibited limited fibrin deposition. The red blood cells were largely intact, with few fragments, and the overall density was reduced. These findings were paralleled by the results of MRI analysis, which demonstrated significant variability in the T1-weighted and T2-weighted signal intensities. The variation in MRI signal intensity corresponded to the differing histologic appearance of the thrombus. These findings suggest that thrombus deposition in the aneurysm remote from the endoleak occurred early after stent-graft deployment excluded antegrade perfusion and that the remote thrombus was relatively stable. In contrast, thrombus in close proximity to the endoleak appeared to be recently deposited, and may have been subject to ongoing remodeling, with repeated cycles of resorption and deposition. Further long-term studies will be necessary to further characterize the relationship of endoleak chronicity and thrombus consistency. It is important to note that significant differences exist between the canine and human coagulation systems. As a consequence of these differences, characterization of thrombus formation must be tempered. In addition, data from the study regarding endoleak patency must also be viewed in light of these coagulation differences.

CONCLUSIONS

The canine model of AAA with a chronically implanted intraluminal pressure transducer enables accurate pressure determination in thrombus over extended periods of implantation. Deployment of a stent graft to exclude the aneurysm from antegrade arterial perfusion results in formation of a retrograde endoleak (type II). Endoleaks originating from retrograde flow in the side branch vessels of the aneurysm generate significant levels of intra-aneurysmal pressure, that is, 70% to 80% of systemic pressure. At least 2 patent side branch vessels appear to be necessary to cause persistent patency of the type II endoleak in the canine model. Further studies will be necessary to enable more complete characterization of retrograde endoleaks and to extend these findings to allow clinical application.

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Submitted May 11, 2004; accepted Jul 29, 2004.